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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,633	01/05/2001	Shumin Yang	IM-2-C1-C1	4819
26949	7590	11/25/2003	EXAMINER	
HESKA CORPORATION INTELLECTUAL PROPERTY DEPT. 1613 PROSPECT PARKWAY FORT COLLINS, CO 80525			KAUSHAL, SUMESH	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 11/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/755,633	YANG ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Sumesh Kaushal Ph.D.	1636	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 July 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 19-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 19-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
     \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
     a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

*Applicant's response filed on 07/07/03 has been acknowledged.*

*Claims 1-18 are canceled.*

*Claims 19-35 are newly filed.*

*Claims 19-35 are pending and are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121 (<http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm>). The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.*

*The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.*

### **Claim Rejections - 35 USC § 112**

Claims 19-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the office action mailed on 03/31/03.

#### **Response to arguments**

Applicant argues that in new Claims 19-35 all references to variants and homologs has been removed. Newly submitted claims recite specified number of nucleotides or amino acid so that regions of identity refers to coding region for IL-5 or to region of IL-5 protein. The applicant believes that submitted claim set is in condition for an allowance (response pages 2-4).

However, this is found NOT persuasive because the scope of newly filed claims encompass any variant of SEQ ID NO: 4, 7, 9 and 18, wherein the variant comprises at

least 45 consecutive nucleotides identical in sequence to 45 contiguous nucleotide region found in SEQ ID NO: 4, 7, 9 and 18. The scope of invention as claimed encompasses variant that is 95% identical to the nucleic acid sequences of SEQ ID NO: 4, 6, 7, 8, 9, 11, 18 and 19. In addition the scope of invention as claimed now encompasses a method of producing a protein encoded by a nucleic acid sequences wherein the nucleic acid encodes a protein comprising at least 20 amino acids identical to a 20 contiguous amino acid region of a sequence from SEQ ID NO: 5 or 10, wherein in the protein elicits an immune response against canine IL-5 protein or IL-5 activity.

Applicant fails to consider the issue raised in the prior office action which clearly states why the a variant which has identity of only 45 consecutive nucleotides or identity of 20 consecutive amino acid or 95% identity fails to meet written description rejection. Applicant were referred to the Interim guidelines on Written Description published December 21, 1999 in the Federal Register, Vol. 64, No. 244, pp. 71427-71440. The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L. P. vs Faulding Inc.* 56 USPQ2nd 1481 (CAFC 2000). At best the instant specification as filed teaches the nucleic acid sequence of SEQ ID NO: 18 and 19 (reverse complement of SEQ ID NO:18) which encodes the amino acid sequences of SEQ ID NO:5 and 10 (Canine IL-5). The specification fails to disclose any variants of nucleic acid sequence of SEQ ID NO: 18 and 19 or nucleic acid encoding the amino acid of SEQ ID NO: 5 and 10 that has any IL-5 like activity explicitly or implicitly as putatively considered by the instant specification. The specification fails to define the minimal structure or consensus core structure that defines the genus comprising nucleotide sequences encoding the amino acid sequences of IL-5. The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. See, e.g., *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568,

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43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406). In the instant case the nucleic acid variants (as claimed) has been defined only by a statement of function that broadly encompasses IL-5 activity or regulation of any components of immune response (humoral or cellular) in any animal (insect, reptiles, amphibians, birds and mammal etc), which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. The variation as claimed also encompasses the conserved motifs, which are considered germane to the functional activity of an IL-5 like polypeptide. For example, 5% variation (95% identical) as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo and Rudinger). Furthermore, the scope of invention as claimed encompasses any variant that does NOT even comprise the conserved amino acid sequences required for the IL-5 activity. Furthermore, considering the scope variants as discussed above it is unclear how one skill in the art would envision an oligonucleotide, recombinant molecule, virus or a cell that comprises the variants as claimed. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this

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genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 19-35 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acid sequences of SEQ ID NO:4, 7, 9 and 18, and method of producing the same, wherein the recombinant protein has Canine IL-5 activity, does not reasonably provide enablement for any natural or non natural variants of SEQ ID NO:4, 7, 9, and 18 obtained from any organisms that has canine IL-5 like activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the same reasons of record as set forth in the office action mailed on 03/31/03.

***Response to arguments***

Applicant argues that in new claims 19-35 all references to variants and homologs has been removed. Newly submitted claims recite specified number of nucleotides or amino acid so that regions of identity refers to coding region for IL-5 or to region of IL-5 protein. The applicant believes that submitted claim set is in condition for an allowance (response pages 2-4).

However, this is found NOT persuasive because the scope of newly filed claims encompass any variant of SEQ ID NO: 4, 7, 9 and 18, wherein the variant comprises at least 45 consecutive nucleotides identical in sequence to 45 contiguous nucleotide region found in SEQ ID NO: 4, 7, 9 and 18. The scope of invention as claimed encompasses variant that is 95% identical to the nucleic acid sequences of SEQ ID NO: 4, 6, 7, 8, 9, 11, 18 and 19. In addition the scope of invention as claimed now encompasses a method of producing a protein encoded by a nucleic acid sequences wherein the nucleic acid encodes a protein comprising at least 20 amino acids identical to a 20 contiguous amino acid region of a sequence from SEQ ID NO:5 or 10, wherein in the protein elicits an immune response against canine IL-5 protein or IL-5 activity.

Applicant fails to consider the issue raised in the prior office action which clearly states why the a variant which has identity of only 45 consecutive nucleotides or identity of 20 consecutive amino acid fails to meet enablement requirements.

**State Of Art And Predictability:** The earlier office action clearly provided the evidence that role of IL-5 in the growth, activation, and survival of eosinophils is complex. IL-5 activates Lyn, Syk, and JAK2 and propagates signals through the Ras-MAPK and JAK-STAT pathways, wherein Lyn, Syk, and JAK2 tyrosine kinases and SHP-2 tyrosine phosphatase are important for eosinophil survival (Adachi et al Am J Physiol Cell Physiol 275: C623-C633, 1998). IL-5 is also known to regulate Th2 immune response. However the regulation and effects of Th2 response in an animal is complex, since it requires a cascade of molecular and cellular interactions among Th2-cytokines (like IL-4, IL-5, IL-9 and IL-13). Th2 cytokine response is involved in immune rejections of parasite helminth infections, allergies and asthma (McKenzie, Pharma. Ther. 88:143-151, 2000). Thus considering the role of multiple cytokines in Th2 immune response, it is unclear how one skill in the art would use any variants of IL-5 (as claimed) to regulate Th2 immune response in any animal. In addition the art at the time of filing clearly teaches that even though IL-5 is a factor that regulate the differentiation and activation of eosinophils in dogs, other factors regulating the differentiation, proliferation and activation of canine eosinophils are not fully understood (Yang et al J Interferon Cytokine Res 21(6):361-7, 2001).

Even though the specification teaches that the polypeptide encoded by the nucleotide sequences of SEQ ID NO:18 encodes Canine IL-5, the specification fails to provide any guidance regarding what are the essential epitopes structure(s) which are considered germane to elicit the required immune response. Even if one skill in the art would be able to generate antibodies against the variants as claimed it is unclear how an antibody raised against such variant would block the canine IL-5 activity. In addition, it is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The

variants as claimed are only hypothetical proteins because no biological function has been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. (see Ngo and Rudinger). The applicant proposes to discover any variant of SEQ ID NO: 4, 7, 9 and 18 by identifying only 45 contiguous nucleotides, 20 contiguous amino acids or 95% sequence identity. For example the variant that encompasses a sequence identity of 45 contiguous nucleotides in SEQ ID NO:18 (1658nt) would be only 2.7% identical (97.3% variation) to SEQ ID NO:18. This renders the invention as claimed unpredictable, since applicant wish to identify a variant that does NOT even comprises the conserved amino acid sequences required for the IL-5 activity (*supra*). The specification as filed fails to disclose any variants of SEQ ID NO: 4, 7, 9, and 18 that encodes a polypeptide having IL-5 like activity explicitly or implicitly as putatively considered by the specification.

**Quantity Of Experimentation Required:** The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). In instant case screening of any and all natural and non-natural variants, wherein at least 5-97% amino acid are added substituted and/or deleted in the disclosed SEQ ID NO:4, 7, 9 and 18 is not considered routine. Making and testing a point mutation is significantly different from the making and testing an amino acid sequences wherein at least 5-97% amino acids are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the requirements for the claimed IL-5 activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in


support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. Therefore, the applicant has not presented enablement commensurate in scope with the claims.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

***S. Kaushal***  
**PATENT EXAMINER**



**JEFFREY FREDMAN**  
**PRIMARY EXAMINER**